Remarks

Claims 1-26 remain pending. Claims 7-10, 13-15, and 17-21 remain withdrawn from consideration. Applicant respectfully submits that claim 1 is generic to these withdrawn claims, and respectfully requests that claims 7-10, 13-15, and 17-21 be examined and found allowable upon indication of the allowability of claim 1. Applicant respectfully requests entry of this response and reconsideration of the rejections.

Applicant acknowledges that the previous response was sufficient to overcome the previous rejections of the claims under 35 U.S.C. § 103.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-5 and 22-24 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabling for RAR antagonists and inverse agonists disclosed other than those disclosed in pages 6-21. Claims 1-6, 11, 12, 16, and 22-26 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventor(s) had possession of the claimed invention.

Applicant respectfully traverses these rejections.

Regarding the enablement rejection, it is unclear as to how the Examiner has issued five other Office Actions and has only now stated that he believes that some of the present claims are not enabled. Applicant respectfully submits that, as implicitly

acknowledged in the five preceding Office Actions, all of the present claims, and claims 1-5 and 22-24 in particular, are properly enabled under 35 U.S.C. § 112, first paragraph.

In addition, the Examiner has stated that the present claims encompass all RAR antagonists or RAR inverse agonists, which would necessitate an exhaustive search for the embodiments suitable to practice the claimed invention. Applicant respectfully submits that whether claims necessitate an exhaustive search is irrelevant in properly establishing an enablement rejection under 35 U.S.C. § 112.

Furthermore, applicant respectfully disagrees with the Examiner's statement that "every compound known to men [sic] would be a potential candidate for the instant invention". Contrary to the Examiner's statement, claim 1 encompasses the use of a RAR antagonist or a RAR inverse agonist. Clearly these two classes of compounds do not indicate that every compound known to man would be a candidate. Among other things, the compounds of the present invention are limited in that they exert an effect on a specific class of receptors (i.e., retinoic acid receptors). Thus, applicant submits that the statement "[o]ne of skilled in the art would then be required to screen every known compounds in order to practice the full scope of the invention" is incorrect and does not support the Examiner's opinion that claims 1-5 and 22-24 are not enabled.

Nevertheless, applicant submits that the specification of the above-identified application provides sufficient guidance to a person of ordinary skill in the art to practice the claimed invention. The claimed invention recites administering a RAR

antagonist or inverse agonist to a patient. The specification discloses how to administer RAR antagonists and inverse agonists to a patient, at least at page 21, line 26 to page 23, line 6. In addition, Examples 1-8 also disclose how to administer an RAR antagonist or inverse agonist to a patient.

In addition, and as acknowledged by the Examiner, the specification includes at least 15 pages (e.g., page 6-21) of examples of suitable RAR antagonists and inverse agonists. Furthermore, the specification refers to, and incorporates by reference, U.S. Patent No. 5,776,699 (Klein et al.) for structures and methods of making RAR antagonists and inverse agonists. Thus, the specification of the above-identified application provides numerous examples of structures and methods of making RAR antagonists and inverse agonists either expressly as described from pages 6-21, and by incorporation by reference to Klein et al. Moreover, at least by the incorporation by reference of Klein et al., the present specification also includes a description of how to assay for RAR antagonist or inverse agonist activity using routine methods known by persons of ordinary skill in the art.

Thus, applicant submits that if any experimentation is necessary to practice the invention, such experimentation would be routine, and would not be undue. Such experimentation would be routine due to amount of direction and guidance found in the present application, including the information disclosed by Klein et al., which was incorporated by reference, the presence of working examples, the state of the prior art, and the substantial level or degree of skill of the ordinary practitioner in the art.

Applicant further submits that although the Examiner appears to suggest that the eight factors discussed *In re Wands* and *Ex parte Forman* are required to assess if a disclosure would require undue experimentation, these factors are not mandatory to determine enablement. In particular, in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d, 1016, 1027, the Federal Circuit states that

> it is not necessary that a court review all the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory. What is relevant depends on the facts …. (emphasis added).

In view of the above, applicant submits that the present specification includes a description of how to make and how to use an RAR antagonist or inverse agonist in accordance with the claimed methods, and in particular, the methods recited in claims 1-5 and 22-24. Thus, applicant respectfully requests that the rejection of claims 1-5 and 22-24 under 35 U.S.C. § 112, first paragraph be withdrawn.

Regarding the rejection of claims 1-6, 11, 12, 16, and 22-26 as allegedly not being properly described in the specification of the above-identified application, applicant respectfully disagrees.

First, applicant submits that the Examiner has implicitly acknowledged that the limitation "without coadministration of a retinoid" is described in the specification. For example, in the June 2, 2003 Office Action at page 3, 2nd full paragraph, the Examiner stated "the new matter rejection is not because the specification fails to describe the coadministration of retinoid

and the compounds herein." Thus, applicant submits that the foregoing remark made by the Examiner is an acknowledgement that the present specification contains a description of administration of a RAR antagonist or inverse agonist without coadministration of a retinoid.

This acknowledgement by the Examiner is fully justified in that the specification contains a clear description that the presently claimed methods are practiced with RAR antagonists or inverse agonists without coadministering retinoids. As indicated in applicant's previous responses, Klein et al. (U.S. Pat. No. 5,776,699) was incorporated by reference into the present application (e.g., see page 6, lines 15-18). Among other things, Klein et al. may be relied upon for its disclosure and teachings of coadministration of retinoids and RAR antagonists or inverse agonists to a patient. In addition, Klein et al. may be relied on for its disclosure of the antagonistic effects mediated by RAR antagonists or inverse agonists with respect to retinoids (see Example 4, Table I). The present application discloses therapeutic effects of RAR antagonists and inverse agonists when they are administered to a patient without the coadministration of retinoids, such as disclosed in Klein.

In addition, as stated in the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, "Written Description" (Federal Register, Vol. 6, No. 4 (2001),

> To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed

> invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, ...
>
> If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.

As indicated in the specification of the above-identified application, Examples 7 and 8 show that the invention was actually reduced to practice. In particular, Example 7 describes that administration of a RAR antagonist or inverse agonist (i.e., AGN 194310) to monkeys resulted in a significant decrease of serum triglycerides. It is clear from Example 7 that the monkeys were not coadministered retinoids. Example 8 describes the administration of a RAR antagonist or inverse agonist to mice results in a decrease of serum triglyceride levels. Again, Example 8 clearly demonstrates that the RAR antagonist or inverse agonist were administered to the mice without coadministering a retinoid. Thus, because the specification includes a description of an actual reduction to practice of the invention, applicant submits that the specification would lead a person of ordinary skill in the art to conclude that the inventors had possession of the claimed invention. Therefore, as discussed in the Written Description Guidelines identified above, applicant submits that the specification of the above-identified application satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

In addition, applicant submits that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. If the Examiner determines that the application does not comply with the written description requirement, the Examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. Applicant respectfully submits that he has not met his burden. Thus, applicant respectfully requests that the Examiner present detailed evidence why a person of ordinary skill in the art would not recognize that the written description of the invention provides support for the present claims, or withdraw the rejection.

In view of the above, applicant submits that the present claims are properly described in the specification to satisfy the requirements of 35 U.S.C. § 112.

Rejections Under 35 U.S.C. § 103

Claims 1-6, 11, 12, 16, and 22-26 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Klein et al. (U.S. Pat. No. 5,776,699) in view of Aberg (Atherosclerosis, 1985), both of which are of record. The Examiner believes that it would have been obvious to one of ordinary skill in the art to employ 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl] benzoic acid in a method of lowering triglyceride level and preventing myocardial infarction because the RAR

antagonists of Klein et al. are known to be useful in inhibiting hypertriglyceridemia.

Applicant respectfully traverses the rejection.

Applicant notes that the current rejection of the claims under 35 U.S.C. § 103 is identical to the rejection set forth in the June 2, 2003 Office Action. On page 2 of the current Office Action, the Examiner has stated that "the outstanding rejection under 35 USC 103(a) **is withdrawn** in view of the amendments filed September 2, 2003 as the claims are drawn to the method of treating hyperlipidemia comprising administering an RAR antagonist [or inverse agonist] without coadministering a retinoid to the mammal" (emphasis added). Thus, applicant submits that the current rejection under 35 U.S.C. § 103 is in error and respectfully requests the rejection be withdrawn.

Nevertheless, applicant submits that because Klein et al. does not specifically teach or even suggest the present invention of treating hyperlipidemia without coadministering retinoids, as recited in the present claims, one of ordinary skill in the art would not be motivated by Klein et al. to use RAR antagonists, including AGN 194310, to treat hyperlipidemia as claimed, let alone be motivated to combine the teachings of Klein et al. with those of Aberg to prevent myocardial infarction. Klein et al. teaches the use of RAR antagonists to treat effects caused by the administration of retinoids and, thus, actually leads away from the methods, as recited in the present claims.

Aberg does not disclose, teach, or even suggest the present invention, and does not supply the deficiencies apparent in Klein et al.

In view of the above, applicant respectfully submits that claims 1-6, 11, 12, and 22-26 are unobvious and patentable over Klein in view of Aberg under 35 U.S.C. § 103.

In addition, applicant submits that each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

In conclusion, applicant has shown that the present claims satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1-26 are allowable. Therefore, applicant requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

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